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THE EFFECT OF ZINC-PROTAMINE-GLUCAGON IN ACUTE PANCREATITIS

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ABSTRACT

A double blind study testing the effect of long-acting zinc-protamine-glucagon (7.5 mg every 12 hours for 4—5 days) was carried out in acute pancreatitis. There were 32 patients in ZP-glucagon- and 39 patients in the placebo group. The results show that glucagon had a slightly favourable effect on the general clinical course of the disease but they do not give enough evidence for routine use of glucagon in pancreatitis.

KEY WORDS: ACUTE PANCREATITIS; GLUCAGON

The generally used conservative treatment of acute pancreatitis consists of anticholinergic drugs, nasogastric tube suction or neutralization of hydrogen ion in the stomach in order to prevent extra stimulation of the already inflammed pancreas.

It is known that glucagon in single dose (0.1—0.2 mg) and in intravenous infusions (0.2 μg/kg/minute) has a similar effect as atrophine on hyperactive gastrointestinal segments (17). On the other hand, it is well agreed that hydrogen ion in the duodenal bulb is one of the most potent stimuli for pancreatic secretion (4, 11).

Apart from decreased H^+-production, glucagon very effectively inhibits gastric motility (7, 12) and consequently prolongs gastric emptying time. Thus the H^+-load at the duodenal bulb is still reduced (9). H^+-stimulus in the duodenal bulb increases both concentrations of exocrine enzymes and the volume of secreted pancreatic juice (10). Glucagon is also known to relax the sphincter of Oddi (13), which might have a beneficial effect on acute pancreatitis. Ductal obstruction caused by pancreatic oedema is considered as one of the factors in the pathogenesis of acute pancreatitis (2). Theoretically the use of glucagon, especially long acting glucagon, seems to be justified in the treatment of acute pancreatitis. The effect of this crystalized zinc-protamine-glucagon is pharmacologically prolonged ($T\,^1/_2 = 4$ hours) as compared to normal glucagon ($T\,^1/_2 = 10$—15 minutes) (13).

MATERIAL AND METHODS

Between March and October 1977 consecutive patients initially diagnosed as acute pancreatitis, were treated with long-acting zinc-protamine-glucagon (»Pla Gluc, Novo Industri A/S) or with placebo in addition to normal conservative treatment with nasogastric tube, i.v. electrolyte solution, anticholinergics and spasmolytics. The investigation was carried out as a double blind study.

The following parameters were recorded twice a day: abdominal pain, general clinical status, urine amylase and leucocyte levels. The need for analgesics was considered as one criterion for pain. Nasogastric aspiration and the need for parenteral treatment were used as parameters when assessing the patient's clinical condition, in addition to usual clinical judgement. During the acute period urine amylase and leucocyte levels were recorded twice a day.

Two patients were operated on for haemorrhagic pancreatitis and were excluded from the study because the treatment was stopped. In seven patients the initial diagnosis of pancreatitis was changed during the course of the disease.

From the 71 patients remaining in the study 28 were women (mean age 53 years) and 43 men (mean age 41 years). The aetiology was considered

small and heterogenic for any definite conclusions to be reached (3, 6, 15, 16). In the present series one patient died and three developed late complications in the placebo group and none in the glucagon group. These numbers, however, are far too small to draw any significant conclusion.

Acute pancreatitis in man encompasses a wide spectrum of clinical varieties with different aetiology, varying in grades of severity and having a very different natural course and prognosis (1).

Accurate clinical diagnosis is sometimes very difficult. Oedematous pancreatitis with a good natural prognosis is often difficult to differentiate even at laparotomy to from early haemorrhagic pancreatic lesions with a high mortality risk.

There is more difficulty and confusion when the parameters used to estimate the effect of any treatment are compared because of their subjective nature such as general condition, abdominal pain etc.. Although this work was performed as a double blind trial the above mentioned risk factors and possibilities to misinterpretation of symptoms and signs must be considered. On the other hand, no side effects were observed when using long-acting zinc-protamine-glucagon.

Because our policy was to operate on patients with haemorrhagic pancreatitis when once suspected, this material consisted of mostly mild to moderate grades of severity of the disease.

In the present study glucagon appears to have had a slightly favourable effect on the general course of this disease especially when gall bladder disease was an aetiological factor, which agrees with previous reports (6, 15, 16). However, in spite of these findings we have not taken glucagon into routine treatment in acute pancreatitis.

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